

**Stereochemical Control of the DNA Binding Affinity, Sequence Specificity, and  
Orientation-Preference of Chiral Hairpin Polyamides in the Minor Groove**

5 The U.S. Government has certain rights to this invention pursuant to Grant Nos.  
GM 26453, 27681, and 47530 awarded by the National Institute of Health.

**CROSS-REFERENCE TO RELATED APPLICATIONS**

This application is a continuation-in-part of PCT/US97/03332 filed February 20,  
1997, Serial No. 08/853,522 filed May 8, 1997 and PCT/US97/12722 filed July 21, 1997  
which are continuation-in-part applications of Serial No. 08/837,524 filed April 21, 1997; *now U.S. Pat 6,143,901;*  
and Serial No. 08/607,078 filed February 26, 1996; *now U.S. Pat 6,090,947;*  
60/042,022, filed April 16, 1997 and provisional application 60/043,444 filed April 8,  
1997. The specification of these applications are incorporated herein by reference.  
*Priority is also claimed to provisional applications: 60/023,309; filed July 31, 1996; 60/024,374; filed*

**BACKGROUND OF THE INVENTION**

**Field of the Invention**

This invention relates to polyamides which bind to pre-determined sites of the  
minor groove of double-stranded DNA.

**Description of the Related Art**

25 The art describes a large variety of polyamides which have three to six  
carboxamide base pairs and a hairpin loop derived from  $\gamma$ -aminobutyric acid and the  
ability to bind to the minor groove of DNA in the promoter region to inhibit gene  
expression. Thus, polyamides consisting of N-methylimidazole (Im), N-methylpyrrole  
(Py), and  $\beta$ -alanine and  $\gamma$ -amino butyric acid and methods for preparation of such  
polyamides are well known.

30 Polyamides containing N-methylpyrrole and N-methylimidazole amino acids are  
synthetic ligands that have an affinity and specificity for DNA comparable to naturally